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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,359	11/13/2003	Yie-Hwa Chang	48483-103186	1306

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/712,359	CHANG ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-18 and 21-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-18 and 21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 06/21/2007 in response to office action mailed on 02/12/2007 has been acknowledged.

Claims 9-18 are amended.

Claims 21-38 are new

Claims 9-18 and 21-38 *are pending and are examined in this office action.*

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action. Applicants declarations under 37CFR § 130, 132 and 132 are fully considered.

Claim Rejections - 35 USC § 112

Claims 9-18, and 21-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of decreasing an eukaryotic cell proliferation in vitro comprising expressing a heterologous polynucleotide encoding a variant of a eukaryotic MetAp2 that lacks aminopeptidase activity, comprises a translation domain and possesses a dominant negative MetAp2 activity, such that the dominant negative activity of said variant metAP2 decreases the proliferation of the cell, it does not enable any variant of MetAp2 and it does not enable decreasing any cell proliferation in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reason of record as set forth in the previous office action mailed on 02/12/2007.

Response to Arguments of 06/21/2007:

Applicant argues claims are enabled for decreasing the proliferation of eukaryotic cells in vivo as well as in vitro. Applicant argues that an example of decrease of yeast cell proliferation by a variant of Met Ap2 is sufficient evidence or support for the instant broad claims that encompass all eukaryotic cells (in vitro and in vivo). Applicant further argues that in vitro results decreased Human Vascular Endothelial (HUVE) cells by expressing a polynucleotide encoding human MetAp2 H231A dominant negative activity is proof of its equivalent efficacy in vivo.

Applicants' arguments however, are found not persuasive because given the broadest reasonable interpretation the invention as claimed embraces cells in live animals including humans and gene therapy and as indicated in the previous action the art is currently unpredictable with regard to any extrapolation of in vitro results to in vivo gene transfers and regarding the use of viral vectors for said gene transfers in vivo. There is a plethora of evidence that the immortalized cultured cells rarely mimic or very poorly represent the cells from which they are originated, to the extent the expression of the resident genes including the integrated transgene/s, if any, is very unlike that of the same in an healthy living animal. Thus the in vitro observations often turn out to be highly inadequate for describing the in vivo situation (Bishop, Reproductive Nutrition and Development 36: 607-616, 1996; p.608 1st col. 2nd¶.). From this it follows that the cell proliferation modulations using coding for dominant negative MetAp2 activity in vitro cultures inadequately represent the expression and behavior of the cells in the intact living healthy animal and therefore an artisan with ordinary skill in the art find that unpredictable. With regard to methods of gene transfers in vivo using both viral and non-viral vectors, as has been claimed in the instant invention, art is still unpredictable with regard to efficacy, specificity and safety. Gene therapy or in vivo gene transfers are still considered to be highly experimental area of research and it has been difficult to predict the out come of any gene and vector systems because of various factors that govern the efficacy and therapeutic potential of the transduced genes, and the undesirable host immune reactions of vectors etc., that occur in vivo. Accordingly, in view of the lack of teachings in the art and lack of guidance provided by the specification with regard to in vivo use of dominant negative mMetAp2 gene transfers and in sufficient number of

examples as of around the filing date of instant application and for the specific reasons cited above, it would have required undue experimentation for one of skill in the art to make and use the full scope of the claimed invention. Hence the rejection is maintained.

NOTE: The Claim dependence indicated for the claim 38 in the claim listing (as on primary claim 35) conflicts with what is indicated in the Applicants argument (as on primary claim 37; See p.23, 5th paragraph). For the purpose of this examination dependence on claim 37 is tentatively considered as valid. Applicant should clarify and make appropriate correction

Conclusion:

Claims 9-18, and 21-36 are not allowed.

Claims 37 & 38 are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

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Patent Examiner
Art Unit 1633

SUMESH KAUSHAL, PH.D.
PRIMARY EXAMINER